ACUTE BACTERIAL MENINGITIS IN THE ZLATIBOR DISTRICT

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SUMMARY: Introduction: Acute bacterial meningitis is present worldwide, with a lethality rate up to 50%. The most common causes are Streptococcus pneumoniae and Neisseria meningitidis. The aim of the research is to analyze acute bacterial meningitis in the Zlatibor district. **Material and methods:** Patients treated at the General Hospital in Uzice were examined retrogradely. Demographic data, risk factors, hematological and biochemical data from blood and cerebrospinal fluid and the findings of computed tomography scan of the endocranium were analyzed. All patients underwent lumbar puncture. The etiological diagnosis was made by identifying the pathogens from cerebrospinal fluid or blood culture. The clinical course was monitored, and the prognosis was determined according to the Glasgow coma scale. **Results:** We examined 148 patients with acute bacterial meningitis (92 men, 56 women), mean age 55.8 +/- 13.1. Half of the patients had comorbidities. In 42%, the possible focus of infection was sinusitis. Main symptoms were headache (100%), fever (97.2%), neck stiffness (95.9%). CSF analysis showed less than 100 polymorphonuclear leukocytes/mm3 in 65% of patients, and CSF protein elevation in 95.3%. 94.6% of patients had leukocytosis in the blood, and 86.5% had elevated C-reactive protein. The most commonly isolated bacterium was Streptococcus pneumoniae (40.5%). 74.3% of patients had a favorable disease outcome. One third of the patients showed epileptic seizures. In 16.2% of patients, the disease ended lethally. Risk factors for lethal outcome were the presence of comorbidities, Streptococcus pneumoniae as the pathogen, the occurrence of epileptic seizures, age over 50 years and male gender. **Conclusion:** The most common cause of acute bacterial meningitis in adult population of the Zlatibor district is Streptococcus pneumoniae, which is also the most common cause of adverse disease outcomes. Majority of patients are men over the age of 50 with comorbidities, which are also a risk group for an unfavorable disease outcome.
Key words:, Acute Meningitis - bacterial; Pneumococcal Meningitis; Acute Meningitis- clinical course; Acute Meningitis- risk factors; Acute Meningitis-disease outcome;

INTRODUCTION

Acute bacterial meningitis (ABM) is an infectious disease with significant morbidity and mortality worldwide. Mortality in untreated patients is up to 50%, in treated 8-15%. Having gone through the disease, 10-20% of patients remain with permanent neurological and mental disorders. [1]. Etiological agents depend on age and geographical area. Streptococcus pneumoniae and Neisseria meningitidis are the most common causes of ABM in adults [2]. Hemophilus influenzae is the cause of ABM at all ages, more common in the population of children up to 5 years of age before the mandatory vaccine [3]. The etiological diagnosis requries isolation of the causative agent from the cerebrospinal fluid (CSF), but meningism is possible with the presence of bacteria in the blood [4]. Predisposing factors for the development of ABM include head trauma, sinusitis, otitis, pharyngitis, pneumonia, but also other immunodeficient conditions such as alcoholism, splenectomy, neurological and hematological diseases.

THE AIM of this study was to analyze the epidemiological characteristics, etiology, risk factors, clinical course and prognosis of acute bacterial meningitis in the adult population in the Zlatibor district.

MATERIAL AND METHODS

The research included patients treated at the Department of Infectious Diseases and the Intensive Care Unit of the General Hospital Uzice, in the period from 1st. January 2009 to 31st

December 2019. Demographic data, risk factors, hematological and biochemical data from blood and CSF, cytological findings of CSF were collected retrospectively. The clinical course and outcome of the disease were analyzed, too.

Hematological and biochemical analyses from blood and CSF were performed by standard methods used in the Republic of Serbia. The etiological diagnosis was made by identifying the causative agent from CSF culture or blood, when CSF culture was negative or unavailable. Samples of CSF were cultured on blood agar plates containing 5% sheep blood and on chocolate agar, incubated in carbon dioxide for 24 - 48 h at 37° C. Isolates of Streptococcus pneumoniae and Neisseriae meningitidis were preliminarily identified based on typical colonial prospects, Gram staining and optochin test for Streptococcus pneumoniae. The Vitek system (bioMérieux, Marcy l'Etoile, France) was used for the final identification and testing of antibiotic susceptibility. The minimum inhibitory concentration test was performed by the E test, according to CLSI guidelines [5].

All patients underwent ophthalmic examination of the fundus and/or computed tomography (CT) scan of the endocranium.

Patients with tuberculous meningitis were excluded from the study.

The outcome of the disease was assessed on the basis of the Glasgow Coma Scale with the following values:

score 1 - death; score 2 - inability of patients to interact with the environment; score 3 - inability of the patient to live independently, but there is an interaction with the environment; score 4 - ability to live independently with incapacity for work; score 5 - working ability. The favorable outcome of the disease was defined by a score of 5, while scores 1 to 4 were marked as an unfavorable outcome [6].

The Statistical Package for Social Sciences SPSS (version 16.0) was used for statistical analysis. A significant difference was represented by P <0.05.

RESULTS

A total of 148 patients with ABM was examined, 92 men and 56 women, aged 22 to 84 years of age, averaged 55.8 +/- 13.1.

A significant number of patients had comorbidities. A third of patients had diabetes and heart disease, 22.3% consumed alcohol excessively. The origin of the infection could be assumed in 88.5% of the patients. Sinusitis was significantly the most common at 41.9%. In 19.6% of patients, ABM was preceded by ear inflammation, in 12.8% by pharyngitis. All patients experienced headache on admission, 97.2% had fever, and 95.9% had neck stiffness during head anteflexion. Vomiting and photophobia were present in 76.3% and 75.6%, respectively. There was no statistically significant difference between the presence of these symptoms.

All patients underwent ophthalmologic examination of the fundus. CT scan of the endocranium was performed in 82.4%. Pathological finding in the sinus cavities was significantly the most common in 41.9%.

Epidemiological characteristics, comorbidities, possible focus of infection, symptoms and findings of CT scan of the endocranium are shown in Table 1.

Table 1. Epidemiological parameters, comorbidities, focus of infection, symptoms and CT scan finding in patients with ABM

Characteristics		ABM No (%)	*P
Age	21-30	9 (6.1)	0.00
	31-40	13 (8.8)	
	41-50	27 (18.2)	
	51-60	49 (33.1)	
	61-70	32 (21.6)	
	71-80	14 (9.5)	
	> 80	4	
Gender	Male	92 (62.2)	0.003
	Female	56 (37.8)	
Comorbidities	Diabetes mellitus	48 (32.4)	0.00
	HTA/CMP	50 (33.8)	
	Asthma/COPD	22 (14.9)	
	Alcoholism	33 (22.3)	

	Neurological diseases	27 (18.2)	
	Psychiatric diseases	9 (6.1)	
	Total	75 (50.7)	0.00
Probable focus of infection	Head trauma	7 (4.7)	0.00
	Otitis	29 (19.6)	
	Sinusitis	62 (41.9)	
	Dental infections	7 (4.7)	
	Pharyngitis	19 (12.8)	
	Pneumonia	9 (6.1)	
Symptoms on admission	Headache	148 (100)	0.06
	Vomiting	113 (76.3)	
	Photophobia	112 (75.6)	
	Neck stiffness	142 (95.9)	
	Fever > 38o	144 (97.2)	
CT scan of the endocranium	Cerebral edema	38 (21.6)	0.00
	Content in the sinuses	62 (41.9)	
	Mastoiditis	6 (4.1)	
	Hydrocephalus	2	
	Recent cerebral infarction	14 (9.5)	

*P - statistical significance for samples ≥ 5

All patients underwent lumbar puncture. The number of polymorphonuclear leukocytes was significantly up to 100/mm3. In a significant majority of patients (95.3%), CSF proteins were elevated, while CSF/blood glucose index was reduced in 40.5% of subjects. The value of protein in the CSF was from 0.22 - 6.1 g / L, on average 2.8 +/- 2.2 g / L.

The most common causes of ABM were Streptococcus pneumoniae and Neisseria meningitidis, in 40.5% and 26.3%, respectively. Other pathogens were significantly rarer.

Serum biochemical parameters of bacterial infection, leukocytosis and elevated C-reactive protein (CRP) level, were observed in a significant number of patients, 94.6% and 86.5%, respectively. The leukocyte count ranged from 5.6 to 16.2x109 / L, averaging 12.4x109/L. The CRP value range was 3.4 - 122 mg/L, averaging 34.1 +/- 45.2 mg / L.

Biochemical findings from blood and cerebrospinal fluid, cytological findings of cerebrospinal fluid and etiological causes of acute bacterial meningitis are shown in Table 2.

Table 2. Biochemical findings of blood and CSF, cytological findings of CSF and etiological agents of ABM

Laboratory parameters		ABM No (%)	P
WBC (x109 /L)	>10	140 (94.6)	0.00
C - reactive protein (mg/L)	>10	128 (86.5)	0.00
CSF polymorphonuclear/mm3	< 100	96 (64.9)	0.00
	100 - 1000	40 (27)	
	> 1000	12 (8.1)	
CSF protein (g/L)	> 0.47	141 (95.3)	0.00
CSF glucose/serum glucose (mmol/L)	< 1/3	60 (40.5)	0.06
CSF isolates	Streptococcus pneumoniae	60 (40.5)	0.00
	Neisseria meningitidis	39 (26.3)	
	Hemophilus influenzae	12 (8.1)	
	Staphylococcus aureus	10 (6.8)	
	Listeria monocytogenes	5 (3.4)	
	Escherichia coli	5 (3.4)	
Blood culture isolates		9 (6.1)	

The clinical course was favorable in a significant majority (74.3%) of the patients. One third of patients had epileptic seizures. In 24 (16.2%) patients the disease ended lethally (Table 3).

Table 3. Clinical course and outcome of patients with ABM

Clinical course of diseases		ABM No (%)	*P
Focal neurological changes		2	
Epileptic seizures		49 (33.1)	0.001
Cardiorespiratory changes		9 (6.1)	0.00
Changes in mental status		4	
Glasgow coma scale at discharge	1	24 (16.2)	0.00
	2	2	
	3	4	
	4	8 (5.4)	
	5	110 (74.3)	

*P - statistical significance for samples ≥ 5

Risk factors for unfavorable disease outcome were further examined (Table 4)

Table 4. Risk factors for unfavorable outcome of ABM

Risk factors	ABM favorable outcome N (%) 110 (74.3)	ABM unfavorable outcome No (%) 38 (25.6)	P
Age > 50	64 (56.4)	35 (86.8)	0.011
Male	80 (52.7)	12 (31.6)	0.020
Comorbidities	46 (41.8)	29 (76.3)	< 0.01
Sinusitis	48 (43.6)	14 (36.8)	0.458
Epileptic seizures	29 (26.4)	20 (52.6)	0.003
WBC (x109 /L) > 10	105 (95.5)	35 (92.1)	0.803
C - reactive protein (mg/L) >10	100 (90.9)	28 (73.7)	0.180
CSF polymorphonuclear/mm3 <100	68 (61.8)	28 (73.7)	0.306
CSF protein (g/L) > 0.47	105 (95.5)	36 (94.7)	0.956
Streptococcus pneumoniae	36 (32.7)	24 (63.2)	0.002

Significant factors for the unfavorable outcome of acute bacterial meningitis were the presence of comorbidities, Streptococcus pneumoniae as the cause of the disease, the occurrence of epileptic seizures, age over 50 and male gender.

DISCUSSION

Analysis of the causes of ABM has indicated differences depending on a wide range of examined age groups in recent years [7].The most common causes are Streptococcus pneumoniae and Neisseria meningitis in adult population, while in children the most common are Streptococcus agalactiae, Escherichia coli, Listeria monocytogenes [8]. Our study included adult population and the frequency of individual pathogens corresponds to the above conclusion of other researchers. Haemophilus influenzae is a childhood pathogen, significantly rarer after the vaccine became mandatory [8]. In our study, it was present in 8.1%, which is expected given that it is the most common colonizer of the respiratory tract mucosa, and especially common in persons with chronic obstructive pulmonary disease [9].

Demographic data showed that men got sick more often, which corresponds to the finding of Diaz and colleagues who proved that men with ABM have more frequent head trauma and excessive alcohol consumption as risk factors [10]. The main risk factor of our patients was hypertension/cardiomyopathy. This can be explained by older age of the patients. Diabetes mellitus was the second most important risk factor. Diabetes leads to changes in body's immune defenses. The function of polymorphonuclear leukocytes is reduced, especially when acidosis is also present. Leukocyte adhesion, chemotaxis, and phagocytosis were also altered and antioxidant bactericidal systems were weakened [11].

Inflammation of the sinuses and ear are more common possible sources of infection in our patients, unlike other studies [12]. This result can be explained by the proven high percentage of bacterial sinusitis in the adult population [13, 14]. This finding is supported by the finding of CT scan, which most often

indicated a pathological process in the sinuses. In addition to headache, neck stiffness and fever with a change in mental status were the most common symptoms of both our study and others. [12]. The clinical course of our patients was accompanied by the occurrence of epileptic seizures in one third of patients. CNS infections as a cause of epilepsy are present in a quarter of patients with ABM [15]. Epileptic seizures have been shown to correlate with lower sugar values and higher protein values in CSF [16]. Risk factors for subsequent unprovoked seizures include focal discharge, sharp electroencephalographic waves, and initial CSF glucose <20 mg / dl [17]. The cytological finding of CSF with pleocytosis with the dominance of polynuclear neutrophils is a standard finding in ABM, which corresponds to our results. Elevated protein values present in a significant majority of our patients are expected findings for bacterial meningitis, although there are data in literature that 1-10% of patients with ABM do not have elevated CSF protein [18]. The value of glucose in CSF was reduced in 40% of our patients. This is consistent with other data describing less than 50% of patients with similar findings. The results indicate the unreliability of this parameter in the diagnosis of bacterial meningitis [19].

The serum parameter of inflammation, C - reactive protein, was elevated in a large percentage of our patients. Browver and coauthors pointed out the unreliability of CRP values in the diagnosis of ABM [20].

The unfavorable clinical course in our patients is smaller than described [12]. The most common cause of death is Streptococcus pneumoniae. The most significant risk factors are advanced age and the presence of comorbidities, which corresponds to the findings of other authors [12]. Our finding is partly consistent with the findings of other authors

who mention the most common age over 65 years [12]. Respondents from Nis authors were mostly of the same age group as ours, with researchers noting that older people often have more sparse symptoms at the beginning of the disease [21]. The authors explain the small percentage of bacterial isolates from CSTs by using antibiotic therapy before taking CSTs. This can delay the diagnosis and adversely affect the further clinical course and outcome of the disease. Interesting are the conclusions of the authors who examined the influence of climatic factors on the occurrence of bacterial meningitis and obtained a positive correlation with the occurrence of wind and fog, and a negative correlation with insolation [22]. It can be assumed that it would be useful to analyze climate data in our patients as well.

CONCLUSION

The expected causative agent of a disease in a patient population is of great importance for each geographical area. The most common cause of acute bacterial meningitis in the adult population of Zlatibor district is Streptococcus pneumoniae, in 40.5% of patients, which is also the most common cause of adverse disease outcomes. The second most common is Neisseria meningitidis (26.3%). ABM is most common in men in their sixth decade of life who have comorbidities. The occurrence of epileptic seizures during ABM is also a risk factor of unfavorable outcomes of disease. The sourse of ABM is most often in the sinuses or ear, so timely treatment of these infections is an important preventive measure. Since there is a vaccine prophylaxis for Streptococcus pneumoniae and Neisseria meningitidis, it is necessary to recommend this preventive measure to the elderly, especially those who have comorbidities.

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